REMARKS:

Claims 1-5 are in the case and presented for consideration.

In response to the Examiner's rejection to claim 4 as being indefinite, claim 4 has been amended to clarify its language. This language is supported by the specification, for example, at page 3, line 27.

Claims 1-5 have also been rejected as being obvious from a combination of U.S. Patent 6,284,277 to Bouloumie et al. (Bouloumie), in view of U.S. Patent 6,063,780 to Dexter et al. (Dexter).

The inventors of the present application looking for the solution according to the present application, ran into difficulties when replacing lactose with an alcoholic sugar of non-animal origin, to eliminate a risk of viral contamination, in a pharmaceutical composition comprising oxaliplatin as active ingredient. These difficulties consisted in that the freeze-drying in vaco of the composition was accompanied by an escape of part of the oxaliplatin from the vials in which the freeze-drying took place, since the alcoholic sugar of non-animal origin itself was probably not able to ensure the cohesion of the dry oxaliplatin matrix being formed during freeze-drying. (See page 3, lines 17-23 for the difficulty and lines 23-30 for the claimed solution.)

Bouloumie teaches a pharmaceutical composition comprising oxaliplatin, mannitol (alcoholic sugar of non-animal origin) and alanine (amino acid). This freeze-drying is not evidently accompanied by the difficulties encountered by the inventors. No such difficulties are mentioned in Bouloumie and the person of ordinary skill in the art, e.g. a chemist specializing in pharmaceutical compositions, would have to discover the difficulty without the help of the prior art. Bouloumie teaches no specific thermal freeze-drying regime from

which it could have been discovered that such difficulties exist.

Since the difficulty discovered by the inventors, that is the escape of oxaliplatin from the vials, is not taught or suggested by the prior art, even if the skilled artisan were to experience these difficulties, the only teaching from Bouloumie which would be relevant is that to solve any such escape problem simply add alanine. The skilled artisan is not taught the conditions which permit the alcoholic sugar of non-animal origin to function as an effective carrier with oxaliplatin to avoid the escape problem.

Taking into consideration that the addition of a further, possibly contaminating substance (alanine), to the composition of oxaliplatin and mannitol (alcoholic sugar of non-animal origin) would have been at odds with the basic aim of the claimed invention (i.e. elimination of the risk of viral contamination), the person of ordinary skill in the art contemplated by 35 U.S.C. 103, could not profit from Bouloumie and would be obliged to look for another solution going beyond the teaching of Bouloumie. The inventors have surprisingly discovered that the difficulties which Bouloumie does not even hint at, can be solved when using a certain specific range of the weight ratio of oxaliplatin to the alcoholic sugar of non-animal origin, in combination with maintaining a specific freeze-drying regime. This solution enabled the substitution of the alcoholic sugar of non-animal origin for lactose without the occurrence of the difficulties they encountered.

In Dexter a freeze-dried composition comprising oxaliplatin and lactose in a weight ratio 1:4.5, for instance, is described. Such composition represented the prior art from which the inventors diverged, in effect, to remove the defects thereof when aspiring to replace the very hazardous lactose (with the viral contamination potential) with the non-hazardous alcoholic sugar of non-animal origin. In this way, it was discovered that the

difficulties did not occur for the combination of oxaliplatin/lactose (see lines 4-6 of page 2 of the present application) as a result of lactose reducing disaccharide (rather than alcoholic sugar-reduction product of monosaccaride) having a chemical structure considerably different from that of alcoholic sugars. In this regard, the ratio mentioned in Dexter (1:4.5) would not have been utilized by the person of ordinary skill in the art, even is such person were working toward the replacement of lactose with the alcoholic sugar of non-animal origin (keeping in mind there is not suggestion or need that that replacement should be made in either reference).

Dexter hence could have provided the person of ordinary skill in the art no suggestion to use its ratio but with the chemicals of Bouloumie. Since the person of ordinary skill would not have been able to use lactose in view of its entagonism with the principal target of the solution of the invention (elimination of the risk of viral contamination), they could not have found this hint useful and would have looked for another solution. As already mentioned, the inventors surprisingly discovered that the difficulties did not occur when using a certain specific range of the weight ratio of oxaliplatin to the alcoholic sugar of non-animal origin, in combination with maintaining a specific freeze-drying regime. This solution enabled the substitution of the alcoholic sugar of non-animal origin for lactose without the occurrence of the difficulties and this would not be obvious under 35 U.S.C. 103 from any combination of Bouloumie and Dexter.

The further conditions, for example, of claim 4 are certainly not obvious from any combination of Bouloumie and Dexter. There is nothing in any of the references to suggest the thermal regimes claimed. While the Examiner points out that there are many different ways to affect this regime, this does not in any way evidence that selecting the claimed

regime, particularly of claim 4 would be obvious to the person having ordinary skill in art as contemplated by 35 U.S.C. 103 or even as suggested by the Supreme Court in *KSR v. Teleflex*.

Simply stating that the selection of regimes is known in general and then using that to evidence the obviousness of a specific regime does not satisfy the *prima facie* showing of obviousness required to properly reject a claim. Nothing in the prior art mentions that just the specific freeze-drying regime according to the present application in combination with the specific weight ratio of oxaliplatin to the alcoholic sugar of non-animal origin leads to any useful result, let alone the elimination of a problem that was discovered by the inventors and not even alluded to in either of the cited references. See, for example, *In re Benno*, 768 F.2d 1340, 226 U.S.P.Q. 683 (Fed. Cir. 1985) where a reference was dismissed by the court where it did not hint at the problem to be solved.

Accordingly, the application and claims are believed to be in condition for allowance and favorable action is respectfully requested.

Respectfully submitted,

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